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NIH title - Improving Adherence and Outcomes by Artificial Intelligence-Adapted Text Messages

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Dates - 04/01/2014 to 03/31/2016, with one-year no-cost extension to March 31, 2017

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Research in this report was supported by the Agency for Healthcare Research and Quality under award number R21-HS022336.

Grant award number - 5R21 HS022336

NCT02454660 Improving Adherence and Outcomes by Artificial Intelligence-Adapted Text Messages (AIM@BP)

Structured abstract (250 words)

Purpose: The objective of this pilot study was to develop a Reinforcement Learning-based mHealth program focused on medication adherence.
Scope: Improving medication adherence requires addressing multiple challenges because patients have a variety of reasons for non-adherence. Studies suggest that 33-50% of patients do not take medications properly, costing about $290 billion.
Methods: A randomized, controlled study with 45 participants was done, with randomization to either (a) Medication Event Monitoring System (MEMS) cap + Text messaging or (b) MEMS only. Individuals in a health plan with a proportion days covered of 0.5 or less were enrolled. Data were collected at baseline, 3 and 6 months. The feasibility of system, adaptation of messages, and self-reported medication and proportion days covered were determined.
Results: At baseline, the study groups were comparable. The reward (pill bottle openings) for the RL agent was impacted by baseline study variables. For example, individuals who indicated that concerns about possible side effects caused them to miss a medication showed a decrease of 14.9% in openings. Learning by the RL agent was also seen, as the distribution of text messages changed over time. By ~1000 decisions, the RL agent had gained experience and the learned weights approached a stable value. Potential efficacy was seen, as self-reported adherence improved at 3 months but not at 6 months. The initial analysis with prescription claims showed no differences in proportion days covered by study group. The RL adaptive text messaging medication adherence system is feasible, is adaptive and may improve medication adherence.

Key Words: medication adherence; reinforcement learning; hypertension

Purpose
The *objective in the proposed pilot study* was to develop a Reinforcement Learning-based mHealth program focused on medication adherence among patients with poorly controlled hypertension. Our *central hypotheses* were that a SMS system that uses Reinforcement Learning (RL) will: be acceptable to patients, adapt to hypertension patients' unique adherence-related needs and preferences and changes in these needs over time, and improve medication adherence and blood pressure control. The specific aims are:

(1) Develop RL methods for adaptive decision-making in human-centered environments and demonstrate the feasibility of the resulting RL-based adaptive SMS medication adherence intervention,
(2) Demonstrate "learning" by the RL-base adaptive system using data showing adaptation of the SMS message stream according to variation across patients and over time in the reasons for non-adherence, and
(3) Examine the potential efficacy of the RL-based adaptive SMS intervention with respect to improvements in medication adherence and systolic blood pressure.

Scope
Self-management of chronic conditions involves complex behaviors, and patients vary in their adherence to these behaviors. The focus of this proposal is medication adherence because patients' failure to take their medications as prescribed is a major cause of excess morbidity and mortality and increased health care costs. Studies suggest that 33-50% of patients do not take their medications properly, contributing to nearly 100,000 premature deaths each year and $290 billion in health care costs. Adherence to antihypertensive medications is of particular importance in its own right, and hypertension can serve as an important tracer condition to better understand and improve medication adherence more generally. Uncontrolled hypertension is a major cause of stroke, coronary heart disease, heart failure and mortality, and medication non-adherence is a major cause of uncontrolled hypertension. For example, in a one-year study of ~5,000 hypertensive patients, most patients took their medications only intermittently with half of patients eventually discontinuing their medications against medical advice.

Improving medication adherence requires addressing multiple challenges because patients typically have a variety of reasons for not taking their medication as prescribed, such as beliefs about their disease and its treatment, organizational challenges, and cost barriers. Moreover, as patients' regimens, health status, and social context change over time, adherence support interventions need to adapt, but most services lack the flexibility to do so.

Mobile health (mHealth) services such as patient text messaging or SMS have shown some promise in improving medication adherence. Mobile text messaging has been shown to improve medication adherence by two-fold, but these studies were of short duration and primarily used self-report. However, many mHealth services are based on deterministic protocols, and these interventions may lack the capacity to meet patients' complex changing needs. As a consequence, these rudimentary systems have demonstrated only effects, but the length of their impact is not clear. One meta-analysis in 2016 reported the median intervention time of such trials was 12 weeks. We propose to apply artificial intelligence (AI) methods, specifically Reinforcement Learning (one type of AI), to develop a model medication adherence system that can automatically adapt SMS communication to improve individual medication taking.

Methods
Study Design. We used a randomized, controlled design with 48 subjects, randomizing subjects to one of two study groups including (a) Medication Event Monitoring System (MEMS) cap + Text messaging , (b) MEMS cap only. We used this design to understand the effect of adaptive SMS messages on medication adherence.

Forty-eight participants received a Medication Event Monitoring System (MEMS) cap, bottle and wireless reader for obtaining objective, real-time information about their adherence behavior. The MEMS hardware consisted of an electronic pill bottle cap, bottle and a wireless unit (roughly the size of a smart phone). When participants placed the MEMS cap on the wireless reader, the data in the cap about date and time the bottle was opened and were transmitted via the wireless reader using Global System for Mobile communications (GSM) to servers managed by AARDEX who makes the device. Participants were instructed how to use each device. Participants returned the devices at the end of the study.

Subjects. We recruited individuals from a commercial plan (Priority Health) who were taking anti-hypertensive medications and who had a medication possession ratio for an antihypertensive medication of *0.5 or less* in the past year. Priority Health produced a list containing the name, address and preferred telephone for these potential participants. We first invited potential participants via mailed letter into the study. The letter was sent from the health plan. Subjects were told in the letter how their name was obtained, briefly described the study and explained that they could phone the health plan study staff to opt-out of a phone call about the study. One week after the mailed letters, health plan staff began telephoning for subject recruitment.

Recruitment. Recruitment began in May 2015 and continued until May 2016. We contacted 1134 individuals and consented 49 subjects (see Consort enrollment and allocation chart). Spectrum Health staff screened all potential participants via telephone to ensure subjects were eligible for the study. To be eligible, participants confirmed the use of an antihypertensive medication and had no history of schizophrenia, dementia, or life-threatening illness. Participants self-reported that they sent or received text messages at least several times per week and had access to internet. RedCap was used to track eligibility of all contacted individuals. If eligible, the health plan staff explained the study and asked subjects if they were willing to participate. If yes, the informed consent documents were mailed to interested, eligible individual. Within 3 business days, individuals were contacted again by telephone by health plan staff to review the informed consent document. Individuals interested and willing to participate returned the signed consent form to the health plan in a postage-paid envelope. At any step, if individuals are neither eligible nor eligible, they were thanked for their time. Every telephone and mail contact was documented in RedCap. Returned, signed consent forms were scanned and emailed to University of Michigan staff via secure email/document sharing server.

Data collection. Baseline and follow-up data were obtained by University of Michigan staff. Baseline data were obtained on the telephone from all participants. Participants were enrolled in the study for 6 months, and each participant received $60 for being in the study. At baseline during the telephone survey, we obtained demographics. We also obtained necessity and concern medication beliefs, illness beliefs and reasons for non-adherence using previously reported and validated survey items. At three months post-recruitment, all participants were asked to complete an on-line survey that asked about their medication use. For participants in the text messaging group, we asked their perceptions of the RL system including satisfaction, its benefits and its limitations. At 6 months post-enrollment, all participants were telephoned to complete the final data collection.

All respondents will have their proportion days covered calculated 6 months before, 6 months during and 6 months after the intervention. At this time, we have data for before and during the study. Priority Health, the health plan partner, will provide to the University of Michigan the prescription claims for all medications for study participants for the period January 2015 through June 2017, so that University of Michigan research staff can align the study inclusion dates for each subject and calculate the proportion days covered. Prescription claims will include variables routinely available on prescription claims, including, for example, patient name, birthdate, generic drug name of drug dispensed, drug strength, quantity dispensed, date and days supply. These data will be used by investigators at the University of Michigan to determine medication possession ratios for the RL agent and as the primary study outcome.

Table 1. Types of SMS Messages and Examples

Disease Beliefs
- Your doctor prescribed blood pressure medication because it's important for your health.
- Be proactive and take charge of your health now by committing to take your blood pressure medication regularly.

Medication Beliefs
- Blood pressure medication is one of the most effective ways you can take control of your health.
- Many side effects lessen or go away in time—you won't feel this way forever, so stick with your medication regimen!

Remember – strategies and cues
- To help you remember, try putting your pillbox or bottles near something you see every day, like your toothbrush.
- Taking your pills even one more day a week can help. Try connecting your pill-taking with a chore to help you remember.

Program Engagement
- We have not heard from you in a few days. Please place the pill bottle cap on the wireless reader.
- Please remember to place your pill bottle cap on the wireless reader next time you take it.

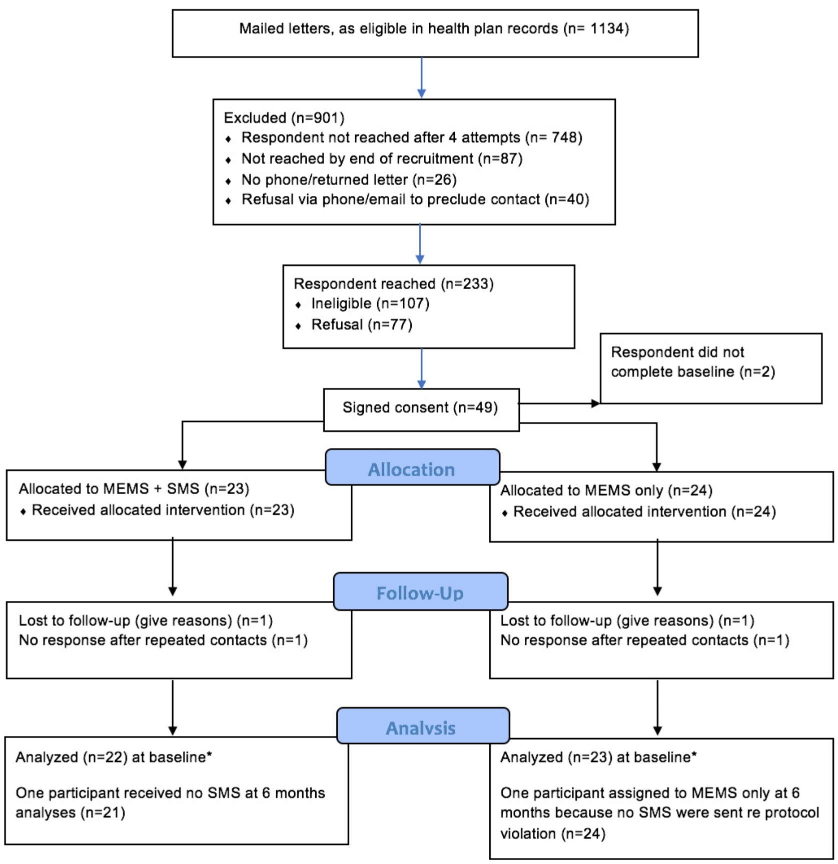
Intervention using The RL system. The system (Appendix 1) included the following components: (a) Website to enroll patients and monitor their experience with the intervention; (b) database of SMS messages organized into categories as shown in Table 1; (c) database that tracks patients' feedback from MEMS caps openings and SMS-reported adherence; (d) service for sending SMS messages to patients' cell phones at designated dates and times; and (e) RL engine that will learn from patients' experience and use RL to decide whether to send a message and what message to send. We used Twilio® for sending and receiving SMS messages. Data sent between the AARDEX server and the College of Engineering servers used unique study identification numbers and no personal health information (PHI). Transfer of information was done using state-of-the-art encryption. SMS messages were not encrypted. The timing of the daily messages (morning, noon, evening or night) was fixed based on when participants reported they usually took their antihypertensive medication. SMS messages were designed by health communication experts to address a variety of major reasons for non-adherence (Table 1). Choice of whether to send an SMS message and if so what message- type to send was made by the RL agent. The RL agent could also determine to send no message.

Analysis. Aim #1. Develop RL methods for adaptive decision-making and demonstrate feasibility of the resulting RL-based adaptive SMS medication adherence intervention via measures of patient engagement. We used descriptive statistics to determine patients' engagement with the system by reporting the number times they opened the pill bottle as measured by the wireless reader and self-reported adherence. We used univariate regression to examine the baseline characteristics of participants with varying levels of engagement. Finally, we used survey data from participants' three- and six-month surveys to understand their satisfaction with the intervention.

Aim #2. Demonstrate "learning" by the RL-based system through adaptation of the SMS message stream according to variation in patient's medication taking over time. We will conduct two different analyses towards this aim. (1) Measuring Change: We will track the number and types of messages sent to participants over the 9 months by study group. We will compare the population's empirical probability distribution across message types during month two (i.e., after the initial increase in adherence attributable to the novelty of the intervention) with the probability distribution in month six in order to evaluate whether the RL-engine adapted its sending of text messages. This analysis will be done for both forms of feedback to the RL system – MEMS and self-report. (2) Cluster Analysis: Finding, or indeed not finding, correspondence between the *a priori* clusters of self-reported reasons for non-adherence and clusters based on what our RL system finds as effective message-types will be a measure of the system's success in adaptation and will provide unprecedented information about "real" reasons for non-adherence among patients with poorly controlled hypertension.

Aim #3. Examine the potential efficacy of the intervention with respect to improving medication adherence. The primary outcome variable will be medication possession ratio. We will compare the medication possession ratio 6 months before the study, 9 months during the study and 6 months after the study. We will use generalized estimating equations (GEE) with repeated measures. Models will include the patient characteristics collected during the study. We expect to see medication non-adherence improve and be associated with changes in patients' beliefs regarding their medicines and their hypertension. Finally, we will determine the extent to which potential intervention effects are associated with patients' baseline characteristics.

Enrollment and Analysis Flow Diagram to MEMS or MEMS + SMS



Results

Table 2. Baseline characteristics of all randomized study participants

Characteristic	MEMS + Text (N=23)	MEMS only (n=24)
	Average (SD)	**Average (SD)**
Age	54.9 (6.6)	55.5 (7.7)
Proportion days covered (1 year before)	0.38 (0.12)	0.41 (0.82)
Number of prescriptions	4.5 (3.0)	5.1 (4.8)
Race (% White)	87.2	91.6%
	Percent	**Percent**
Education		
High school or less	30.4%	20.8%
Some college or more	69.6%	79.2%
Marital status		
Married	87.0%	83.3%
Employment status		
Full-time	65.2%	75%
Income		
Up to $50,000	4.3%	4.2%
$50,001 to $100,000	56.5%	45.8%
> $100,000	34.8%	45.8%
Health Literacy (% never need help reading instructions)	82.6%	83.3%
Self-reported adherence (% excellent)	69.6%	83.3%
Self-reported adherence (% excellent or very good)	83.3%	91.7%

Participants. Individuals consented by health plan staff numbered 49, and 47 individuals were randomized into the study, with 45 individuals completing the study at 6 months. One individual randomized to receive SMS never received them and we categorized that participant as MEMS only at 6 months. (see Consort recruitment and allocation figure above). We contacted 1134 individuals who met the study inclusion criteria of covered at Priority Health and had 0.5 or less PDC in past year for an anti-hypertensive medication. Individuals were contacted by letter and 40 individuals opted-out of further contact. Study staff reached 233 individuals by phone to further assess their eligibility and 49 individuals met study inclusion criteria and consented to participate. When we contacted individuals to collect baseline data within one week, we were reached 47 individuals who were randomized into the two study groups. Two individuals were lost to follow-up. Analysis at 6 months included 45 individuals.

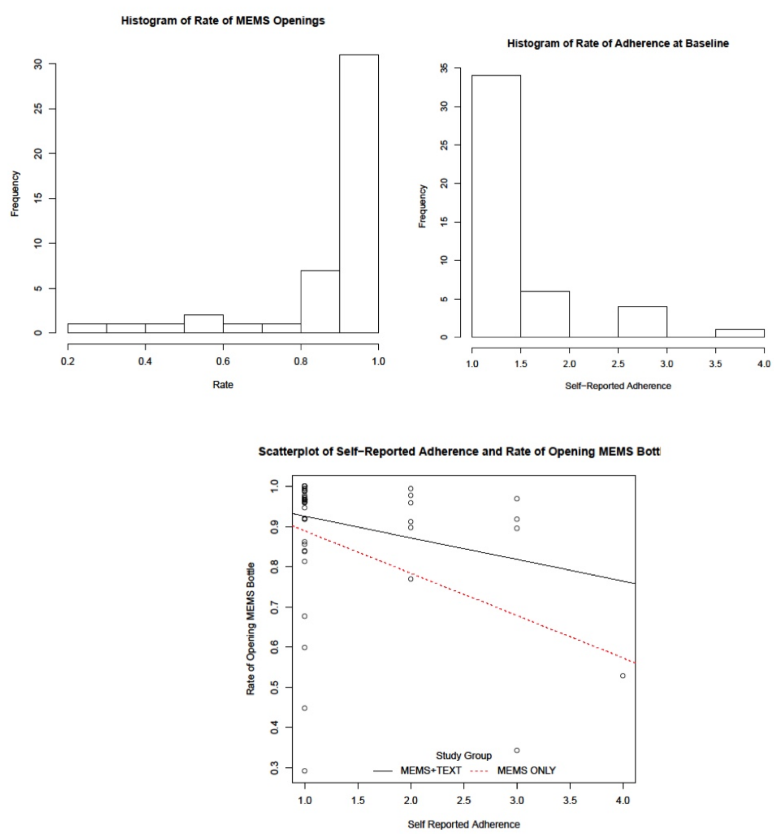
At baseline, the two study groups were comparable (Table 2) and no statistically significant differences were noted. The proportion days covered was indeed less than 0.5 for the anti-hypertensive medication and each group consumed an average of almost five medications. Self-reported adherence was asked “Thinking about the past 4 weeks, please rate your ability to take your blood pressure medication as prescribed”, using a 1 (excellent) to 5 (poor) scale. The proportion reporting excellent was almost 70% in the MEMS +Text group and 83.3% in the MEMS only group, but this difference was not statistically different.

Principle findings

<u>Aim #1. Develop RL methods for adaptive decision-making and demonstrate feasibility of the resulting RL-based adaptive SMS medication adherence intervention via measures of patient engagement</u>.

An RL-based adaptive SMS medication adherence intervention was feasible as evidenced by pill bottle openings and its association with other study variables. The RL agent reward was pill bottle openings, and the mean pill bottle openings, on a scale of 0.0 to 1.0 over the entire 6 month study period was 0.88 (standard deviation 0.18) and median was 0.96, indicating a high proportion of pill bottle openings. The mean self-reported medication adherence (1=excellent and 5=poor) at baseline was 1.378 (s.d. 0.75) and Median was 1.0, also indicating high medication adherence. In examining the pill bottle openings across the entire study by study group and baseline self-reported adherence, the MEMS + Text group appeared to have better pill bottle openings (Figure 1, bottom panel).

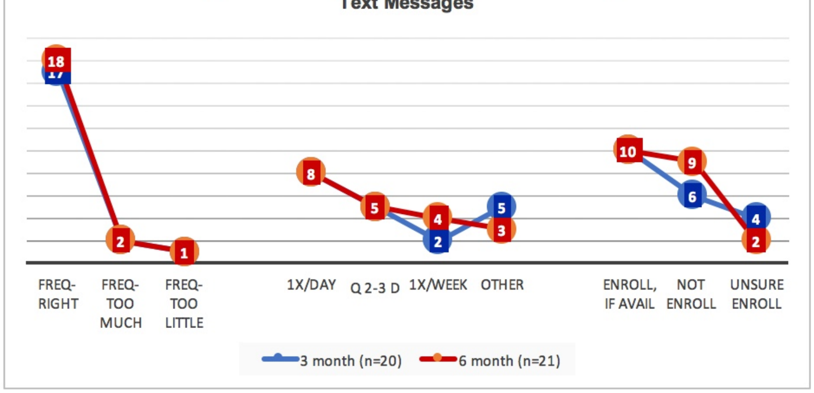
Figure 1. Histograms of MEMS openings and self-reported adherence



We examined the impact of medication beliefs at baseline on pill bottle openings throughout the study using univariate regression. For each one-point increase in concern beliefs, there was a 1.2% increase in the pill bottle opening rate [exp(Estimate) 1.012, $p<0.001$]. A single unit increase in necessity beliefs showed a 0.7% increase in the pill bottle opening rate [exp(Estimate) 1.007, $p<0.005$]. We asked about twelve different reasons for medication non-adherence, and individuals indicated whether a reason was the cause of missed medications in the past 4 weeks. Among individuals who indicated that concerns about possible side effects caused them to miss a medication, there was a decrease of 14.9% (1-0.851, $p=0.008$) in the number of pill bottle openings. Among individuals indicating that they missed a medication in the past 4 weeks due to a busy schedule, there was a decrease of 20.1% (1-0.799, $p<0.001$) in the number of pill bottle openings. For the people who “simply missed it”, there was a corresponding decrease in number of pill bottle openings of 14.4% ($p<0.001$). The number of conditions was also a significant negative predictor. For each extra condition, there was a corresponding decresase in the average pill bottle opening rate of 3.7% ($p<0.001$). These data indicate that the RL-based adaptive SMS medication adherence system had a “reward” that was impacted by baseline variables.

Finally, feasibility of the RL-based adaptive SMS medication adherence intervention was also shown by considering the responses of participants to questions about their interaction with the intervention.

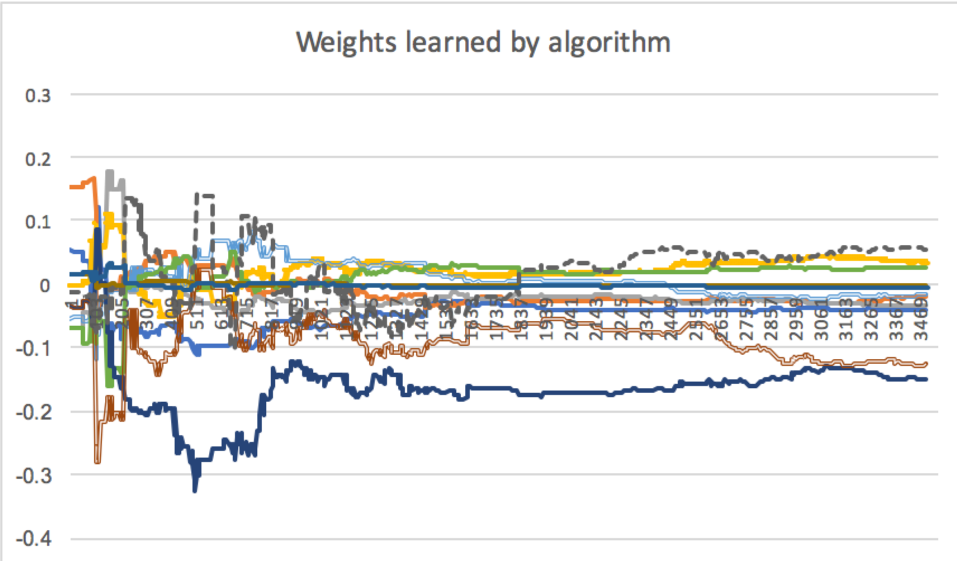
Figure 2. Feedback from Participants Receiving Text Messages



Participants receiving the Texts were asked about the frequency of messaging and if they would enroll in a similar program. At 3 and 6 months, the majority of individuals thought the frequency of messaging was about right. Almost 50% of participants in the MEMS + Text group would enroll in a program offering text messaging about their medications.

Aim #2. Demonstrate "learning" by the RL-based system through adaptation of the SMS message stream according to variation in patient's medication taking over time.

Figure 3. Weights learned by the RL agent from interacting with the population of patients



The reinforcement learning agent used an algorithm known as LinUCB to determine which message-type to send each day to the participants. This algorithm uses context, which is a representation of how the participants have responded so far to each message-type they received. This allows the agent to personalize learning towards the individual patient it is making a decision for, while sharing data across the population in order to learn faster. The agent learns weights to assign to each feature of the context vector. The context vector was operationalized using a method known as tile coding, which allows the agent to learn the weights faster. Figure 3 shows some of the weights learned by the agent. The x-axis represents the number of decisions made across the population, and by about 1000 decisions made, the agent had gained enough experience that the weights learned were approaching a stable value. This shows that even though the majority of patients were highly adherent, the agent was still able to learn from interacting with these patients.

The RL agent was established with a bias towards choosing the no message. In other words, if there were a set of message-types that appeared equally good to the RL agent, and the no message option was among them, then the agent always chose the no message option. This was done so as to not overburden participants with messages. Since the population of patients was mostly highly adherent and they took their medication regardless of what message-type was sent, the agent learned to mostly *not* send messages. In the first month when the agent was deciding which message-types to send, it chose to not send a message for 43% of the days. By month 3, that number rose to 65% and by month 6, it was approximately 80%. These distributions of message-types are shown in Figure 4.

Figure 4. Distribution of SMS at baseline, 3 months and 6 months.

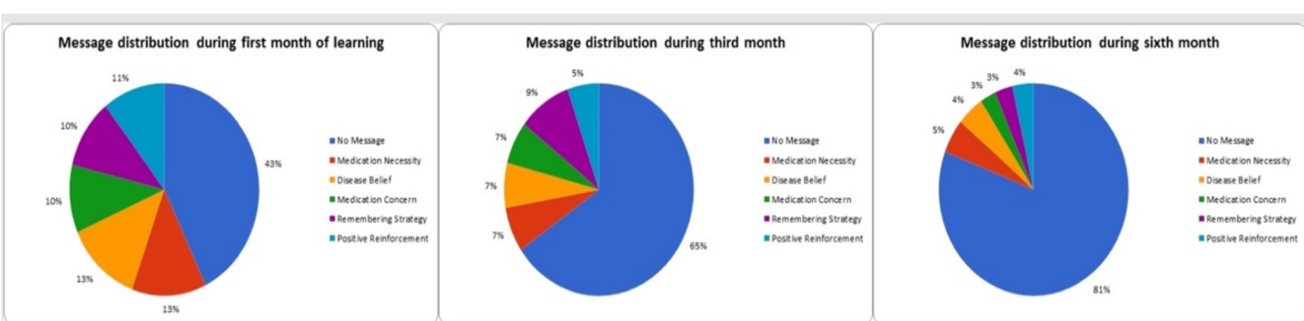


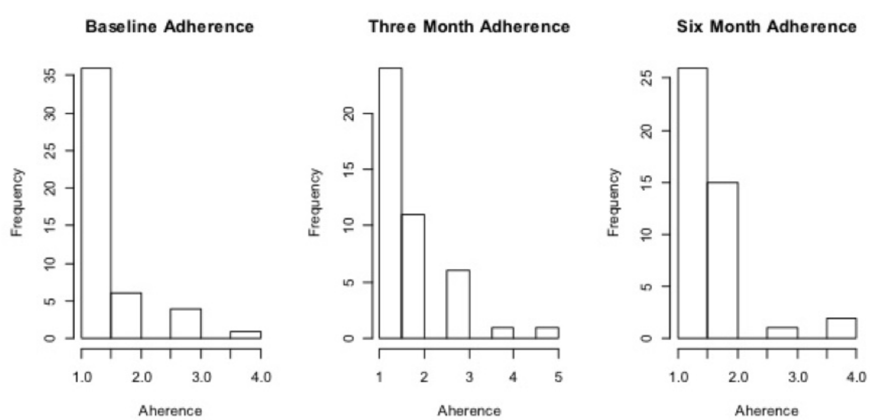
Table 3. Clustering of participants according to their response rates to message-types that targeted underlying non-adherence beliefs

Study ID	Cluster	Overall Adherence Rate	Medication Necessity	Disease Belief	Medication Concern	Remembering Strategy
1	1	98%	92%	100%	92%	93%
5	2	84%	89%	77%	75%	83%
6	3	100%	100%	100%	100%	100%
8	2	78%	80%	67%	88%	71%
10	3	100%	100%	100%	100%	100%
11	4	32%	25%	29%	40%	38%
12	5	92%	100%	89%	83%	100%
15	1	99%	91%	100%	100%	94%
17	5	92%	100%	87%	88%	94%
19	1	95%	88%	91%	93%	94%
20	3	100%	100%	100%	100%	100%
24	1	99%	100%	100%	95%	93%
27	1	97%	92%	100%	90%	86%
30	1	92%	92%	88%	93%	94%
35	1	94%	94%	91%	95%	89%
37	1	96%	95%	92%	96%	95%
38	1	97%	94%	95%	100%	94%
41	1	96%	93%	94%	94%	96%
42	3	100%	100%	100%	100%	100%
44	5	97%	100%	93%	92%	94%
48	1	97%	93%	100%	89%	100%

The characterizing feature of the participants who received text messages is that they were mostly adherent. Of the 21 participants who received text messages, only two had an adherence rate below 80%. This high rate of adherence across the population reduced the differences between patients in how they responded to different message-types, because in most cases, they responded almost equally well upon receiving each type of message. However, it was still possible to observe clusters among participants based upon their response rates to each message-type. Five clusters were observed including one cluster that was highly different from the other four (Table 3), and this cluster contained one participant whose adherence rate was very different from the others. Table 3 shows the five clusters as well as pill bottle openings/adherence rates to the different message-types which addressed underlying reasons for non-adherence - medication necessity, disease belief, medication concern and remembering strategy messages. Overall, pill bottle openings were very high for each participant in the MEMS + Text group, although there was some variability in pill bottle opening by message type for participants.

Aim #3. Examine the potential efficacy of the intervention with respect to improving medication adherence.

Figure 5. Self-reported medication adherence at 3 and 6 months and change by study group



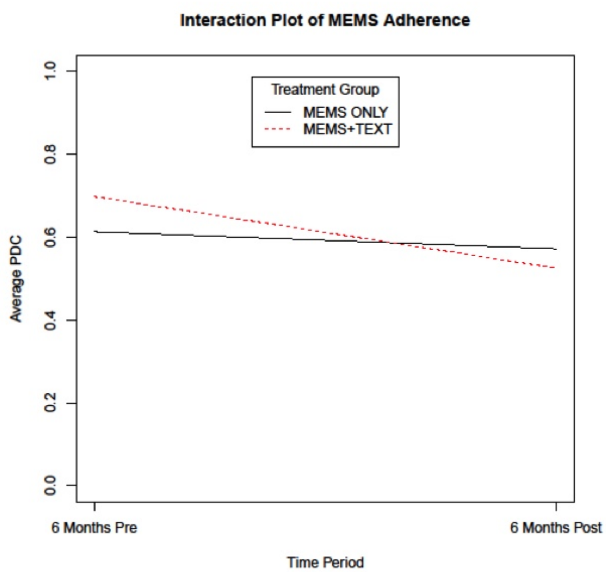
	MEMS + Text	MEMS only*	
Adherence rating difference (E,VG,G,F,P)			
Baseline to 3 months	0 (1.1)	0.68 (1.0)	t=2.04, p=0.04
Baseline to 6 months	0 (1.0)	0.36 (0.85)	t=1.28, p=0.20

*The mean difference is higher in MEMS, therefore adherence worsened.

Two measures of medication adherence were examined as outcomes for this study. Self-reported medication adherence where 1=excellent and 5=poor was assessed at baseline 3 and 6 months. Change in self-reported medication adherence from baseline was compared by study group using a t-test. Medication adherence improved in the MEMS + Text group at 3 months (p=0.04) but not at 6 months (p=0.20).

In considering the proportion days covered (PDC), we have 6 months before the study and 6 months during the study at this time. We have requested the claims for the 6 month period following the study and they will be received by mid-August. We will submit an addendum to this report for that final analysis. The PDCs from the 6 month prior to the intervention were compared to the period 6 months during the intervention. In addition, these values stratified by the treatment group, either MEMS only or MEMS + Text. The PDCs were low, ranging from 0.52 to 0.69, and do not appear to be congruent with the pill bottle opening data. Both study groups showed reductions in PDCs for the periods 6 months before study participation and 6 months during study participation.

Figure 6. PDC for 6 months prior and 6 months during the study



Time Period	Treatment Group	Mean PDC
Pre- 6 Months	MEMS ONLY	0.613 (sd=0.164)
Post- 6 Months (during the study_	MEMS ONLY	0.572 (sd=0.151)
Pre- 6 Months	MEMS+TEXT	0.698 (sd=0.216)
Post- 6 Months (during the study)	MEMS+TEXT	0.525 (sd=0.165)

At this time, a repeated linear regression was conducted on the PDCs and the interaction term between treatment period and treatment group overall was not significant (p=0.13). A pairwise analysis of the interaction revealed that the decrease in PDC within the treatment group was significant (p=0.0336, adjusted with the Tukey-Kramer method for post-hoc comparisons) (Figure 5). This finding was surprising, given the self-report and pill bottle opening data. These analyses will be re-run when the entire prescription claims dataset is obtained from the health plan.

We considered whether the text messages might have an effect on medication beliefs, as some of the messages were focused in this area. Medication necessity and concern beliefs were assessed and computed, where the score ranges from 5 to 25. A higher necessity belief score is associated with better medication adherence and higher concern belief score is associated with poorer medication adherence. In terms of medication necessity beliefs, there was no statistically significant difference between groups over time (t = 0.57659, df = 42, p = 0.56). MEMS + Text group had a stable score from baseline to 6 months [17.61 (3.83) to 17.68 (3.44)], whereas the MEMS only group showed a slight increase from 19.33 (4.74) to 20.26 (4.16). In terms of medication concern beliefs, the MEMS + Text group showed a decrease in medication concern beliefs from baseline to 6 months [11.3 (3.21) to 10.27 (3.49)], while the MEMS only group showed an increase [9.75 (3.37) to 10.43 (3.53)], but this change over time between groups was not statistically significantly different (t = 1.61, df = 42, p = 0.11).

Outcomes

- An RL agent was established that was able to adapt the distribution of text messages sent to study participants. The system used pill bottle openings as the reward for the RL agent and the agent chose a text message or no message each day for participants in the MEMS + Text group. The RL-based adaptive SMS medication adherence intervention was feasible as evidenced by pill bottle openings and its association with baseline study variables such as medication necessity beliefs and experience side effects as a reason for missing doses.
- Learning by the RL agent was seen, as the distribution of text messages changed over time, indicating that the RL agent adapted text messages. This adaption occurred, even though there was less than expected variation in the reward or pill bottle openings. Using RL adapted text messages is feasible.
- Further, participants indicated that one message per day or one every 2-3 days was generally preferred. About half of the participants receiving text messages would enroll in a text-messaging service, and this sentiment was the same at 3 and 6 months
- In terms of the potential effect of adapted text messages, self-reported adherence improved at 3 months but not at 6 months. Our initial analyses with prescription claims showed a reduction of poorer medication adherence in the MEMS + Text study group, but both groups had poor medication adherence and both groups showed decreases. These data are in stark contrast to the pill bottle opening data for a similar time frame. Our data request for the final set of data has been submitted, and we expect the data by mid-August. Further analyses in this area is necessary.
- Proportion days covered was used to generate a list of individuals who were eligible for the study and who had a proportion days covered of 0.5 or less. Estimates of proportion days covered from the health plan were not congruent with subsequent data from pill bottle openings which were very good for all study participants.

Discussion

Feasibility. A technological system was developed that is able to adapt its "intervention" over time to support individuals taking medications. The intervention is this study was sending text messages. For an individual, the system requires special pill bottles with wireless technology as well as a phone that receives text messages. For a health plan or health system, this system requires an enrollment database, bank of text messages, RL agent, text messaging format/provider as well as the items required for participants. In this study, there were few, if any, glitches or problems with the text messaging provider. Because the RL agent requires a timely reward, pill bottle openings with wireless technology were used so that daily feedback was available for the RL agent. The RL agent used the opening (or not) as the response/reward from the action it took (sending a message or no message).

In terms of feasibility, there were a limited number of problems with the pill bottle in terms of wireless connectivity, and, even with some problems, the technology maintained the data and we received the data when the wireless was back online. The pill bottle technology itself is somewhat awkward as it requires the participant to place the bottle on the wireless reader. Improved bottle technology that is available today that requires no additional behavior from participants should be considered in future studies.

One important issue in terms of feasibility is whether pill bottle openings is sufficient as a reward. For example, when pill bottle opening is very common, as in this study, then it is less able to distinguish which messages work. As we biased the RL agent to send no message, this became the predominant response. Moving forward, the reward appears to need more variability, which can be achieved with a different reward or having individuals in the study with more variable medication adherence.

Significantly more variation in pill bottle openings was expected because the proportion days covered in the prescription claims was so low at 0.5 or less.

In terms of feasibility, the text messages and system were accepted by study participants. As well, almost half of the individuals in the MEM + Text group were interested in enrolling in a similar program.

Impact. We sought to determine the potential efficacy of the RL adaptive text messaging system. Self-reported medication adherence improved at 3 months, compared to the control group. The improvement was small yet statistically significant in this trial with 48 individuals. It may be that participants receiving text messages experienced heightened awareness of their medication use due to the text messages. As both groups used the pill bottle, this change is not attributable to the MEMS. While no statistically significant changes were seen in medication beliefs between the two study groups, trends were in the correct direction for medication concern beliefs (p=0.11). Given the preliminary consideration of this variable, this finding is positive.

The proportion days covered data is concerning. First, the eligibility criterion was that potential participants should have a proportion days covered of 0.5 or less in the past year for his/her anti-hypertensive medication. We consented individuals into the study based upon this list. Second, self-reported baseline data did indicate very good medication adherence rates. Yet, it was difficult to consider that the proportion days covered could be so far off, and we proceeding as if we were the health plan and we were recruiting non-adherent participants. Third, as the pill bottle opening data began to be examined over the first few months of the study, it became evident that the proportion days covered data was not aligned with either self-report pill bottle opening. In fact, self-report and pill bottle opening were similar. We will obtain 18 months of prescription claims data for all study participants and examine these data again. This issue requires significantly more time to analyze and to consider the data quality of prescription claims.

Next steps. The RL adaptive text messaging medication adherence system is feasible, is adaptive and may improve medication adherence. To further test its impact, it requires that it be deployed in a population with significantly more variation in medication adherence. It is preferred that it be deployed in population with poor medication adherence, as that is the group of individuals who needs the intervention most.

Limitations. The participants enrolled in the study were effective in establishing the feasibility and acceptability of the RL adaptive text messaging medication adherence system. Even with their very good medication adherence, a change in self-reported medication adherence was seen at 3 months. Further analysis with a new pull of prescription claims will be conducted to gain further insights into the possible efficacy of the system. The system, in its current form, is not two-way and its design should be improved to accommodate two-way communication with participants.

Conclusions

The RL adaptive text messaging medication adherence system is feasible, is adaptive and may improve medication adherence.

Significance

Self-management of chronic conditions involves complex behaviors, and patients vary in their adherence to these behaviors. Studies suggest that 33-50% of patients do not take their medications properly, contributing to nearly 100,000 premature deaths each year and $290 billion in health care costs. Text messaging is an easy way to remind, communicate messages about medications and interact with individuals. Text messaging has now been shown to improve self-reported medication adherence in several studies, but over short periods of time. The latter is critical and requires adaptive messaging. Further, pill bottle technology has improved, even since the initiation of this project. Thus, the RL adaptive text messaging medication adherence system is an important development. Its application in the “right” population requires further study. Adapting SMS is a promising approach that requires implementation considerations in the real-world not in controlled trials because of the artificial circumstances in trials that impact medication adherence.

Implications

- Future real-world deployment using observational designs to study the RL adaptive text messaging medication adherence system should be pursued.
- The population for deployment must have variable medication adherence for the intervention to be potentially effective. Individuals with high cost medications or with high prevalence of side effects are potential populations where impact could be determined.

List of Publications and Products (Bibliography of Published Works and Electronic Resources from Study)

In process

Farris KB, Piette JP, Newman S, Marshall V, Batra P, Salgado T, Singh S. Impact of adaptive text messaging on medication adherence to anti-hypertensives: an RCT

Farris KB, Piette JP, Newman S, Marshall V, Singh S Lack of congruence between proportion days covered and pill bottle openings

Invited Presentations

Farris KB, Piette JP, Newman S, Batra P, Salgado T, Singh S. mHealth Technology to Improve Medication Adherence. Society of Behavioral Medicine, San Diego, CA, March 29 - April 1, 2017.